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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,228	07/08/2003	Mark S. Chee	1091.1C	1818

22886 7590 03/20/2006

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EXAMINER

WHALEY, PABLO S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 03/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,228	CHEE ET AL.	
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-45 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 36-45 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>5/10/04</u> . | 6) <input type="checkbox"/> Other: ____ |

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DETAILED ACTION

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 36-45. Claims 1-35 have been canceled.

OBJECTIONS

Claim 36 and 41 are objected to because of the following informalities: Claim 36 and 41 contain typographical errors, and should recite "in the library..." (line 8). Appropriate correction is required.

NEW MATTER

The amendment filed 08/09/2004 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The incorporation of the priority documents into the specification, as added in the Transmittal letter filed 7/8/2003, are new matter as they were not filed with the original disclosure. Applicant is required to cancel the new matter in the reply to this Office Action.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 36-40 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 36-40 are directed to a method of identifying mutations in sample nucleic acid sequence that does not recite either a physical transformation of matter nor a practical application. For example, instant claim 36 recites steps of "comparing" and "identifying." Claim 36, however, does not result in a physical transformation of matter. Processes may be statutory where they recite a concrete, tangible, and useful result (i.e. a practical application). No actual, concrete result is recited in the claims, nor is any useful result "produced" in a tangible form useful to one skilled in the art. For these reasons, the claims are not statutory. See the Guidelines for Patent Eligible Subject Matter (USPTO, 1300 OG 142, Nov. 22, 2005).

Claims 41-45 are drawn to a computer product containing computer-code (i.e. a program). A program, per se, is nonstatutory. Claim 41 further recites the limitation of a "computer read code that store a plurality of patterns in a library." It is noted that Fig. 1, Fig. 2, and Fig. 3 disclose components of a computer system drawn to memory; however, it is not clear that these are intended to be a description of a "library." For these reasons, the "library" for storing a plurality of patterns is not interpreted to be a physical element of the method claimed. As no definition for "library" was provided in the Specification, it is unclear whether this term is intended to be a database or otherwise (See below). A database, even when carried on a

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physical medium, is nonfunctional descriptive material, and is not statutory subject matter. A combination of a database and a program does not render either statutory. For the reasons set forth above, the claims are not statutory. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter at 1300 OG 142, Annex IV, Nov. 22, 2005.

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 36-45 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying mutations by comparison of patterns of samples with "known" mutations does not reasonably provide enablement for identifying mutations by comparison to patterns of random samples. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

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prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below which leads to the determination that the above claim lacks enablement due to undue experimentation being required to make and use the invention.

In the instant case, the claimed subject matter, drawn to a method and computer program product for identifying mutations in a sample nucleic acid sequence, lacks enablement for the following reasons:

- Given the nature of the invention, identifying mutations in a sample nucleic acid sequence requires that the sample sequence be compared to a sequence with at least one known mutation, where a subsequent “match” determines the presence of a mutation. However, there is no such limitation in the instant claims. [Wands factors (2), (4), (8)].
- The method of Claim 36 generally results in the identification of a mutation in a nucleic acid sequence according to a match with a pattern in the library. However, while the specification does exemplify methods of mutation identification by performing base calling methods within a “bubble” [p.45-47], this example does not provide sufficient guidance as to how to identify mutations based on pattern matching to random samples (i.e. those without “known” mutations). [Wands factors (2), (3)].
- Claim 36 and 41 recite the limitation of “identifying a mutation in the sample nucleic acid sequence according to a match with a pattern in the library.” However, there is no recited relationship between the “patterns” of nucleic acid sequences and a “mutation.” Methods and programs for identifying mutations in nucleic acid sequences well-known in the art include methods such as nucleic acid screening on gene chips, where

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hybridization intensities of reference nucleic acid sequences with known mutations are compared to sample nucleic acid sequences (Webster et al., US Pat. 6,600,996). Despite the high level of skill in the art, as the steps of the instant claims do not recite any sort of comparison to patterns, samples, etc. known to comprise mutations, one skilled in the art would not know how to identify a mutation by "matching" patterns in a library derived from samples of unknown provenance, therefore it would require undue experimentation by one of skill in the art to predictably practice the instantly claimed invention. [Wands factors (1), (2), (6), (7)].

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 41 recite the limitation of "a pattern" (line 8). Claim 36 provides a definition for the term "pattern", however it is unclear whether a "pattern" is an actual sequence, a motif, base positions, or otherwise. It is further unclear in what way "probe intensities reflecting hybridization affinity" further limits each "pattern." Clarification is requested.

Claims 36 and 41 recite the limitation of "patterns in a library" (line 8). It is unclear whether these are the previously stored patterns (line 3), new patterns, subsequently added patterns, or otherwise. Clarification is requested.

Claims 36 and 41 recite the limitation of "a pattern" (line 13). It is unclear whether "a pattern" corresponds to a reference nucleic acid sequence, a sample nucleic acid sequence, a first nucleic acid sequence, a second nucleic acid sequence, or otherwise. Clarification is requested.

Claims 37 and 42 recite the limitation "destabilization". It is unclear as to the intended meaning of "destabilization" as it relates to base positions. Clarification is requested.

Claims 37 and 42 recite the limitation "shape of the patterns". It is unclear as to the intended meaning of "shape" as it relates to base patterns. Clarification is requested.

Claims 39 and 44 recite the limitation "wherein probes corresponding to the probe intensities have a length and an interrogation position". It is unclear in what way this limitation further limits the method of Claim 36. Clarification is requested.

Claims 40 and 45 recite the limitation "wherein the base position....is identified utilizing the length of the probes and the interrogation position". As written, it is unclear what part of this method is the active step. It is further unclear what step(s) are intended to be encompassed by the term "utilizing" (line 2). Clarification is requested.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 36-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Webster et al. (US 6,600,996; Priority: Oct. 21, 1994)

Webster et al. teach computer-implemented methods for analyzing biological sequences of nucleic acids in order to monitor changes in gene expression [Abstract]. More specifically, Webster et al. teach the following aspects of the instantly claimed invention:

- Gene chips consisting of standard and alternate groups corresponding to probes complementary to a reference and sample sequence at various base positions [Fig. 9][Col. 7, lines 19-30], which correlates to a "plurality of patterns in a library" as in instant claims 36 and 41.

- Receiving and comparing hybridization intensities of “perfect match” and “mismatch” probes that are covalently attached to the chip [Col. 17, lines 21-37] [Fig. 18], which correlates to “comparing patterns to patterns in a library” as in instant claims 36 and 41. Computer system utilizes the layout information and the fluorescence information to evaluate the hybridized nucleic acid probes on the chip (i.e. library) to identify mutant targets and their genetic sequence [Col. 8, lines 1-6] [Fig. 4, Step 212], as in instant claims 36 and 41.
- Variations in fluorescent intensities (i.e. patterns) at different interrogation positions (i.e. base positions) in a region [Col. 9, lines 25-40] and [Fig. 22], which correlates to “destabilization associated with different bases” as in instant claims 37 and 42.
- Probe intensities reflecting hybridization of wild-type probes [Fig. 8], as in instant claims 38 and 43.
- Probes interrogation positions [Col. 14, lines 45-50], as in instant claims 39 and 44.
- Mutations are identified using fluorescence information from probes of specific length [Col. 17, lines 56-62] at specific locations (i.e. interrogation positions) [Col. 8, lines 1-6], which correlates to “utilizing the length of the probes and the interrogation position” as in instant claims 40 and 45.
- Computer products and code to carry out the above methods [Col.4, lines 62-67] and [Col.5, lines 1-7], as in instant claims 41-45.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 5:30pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
3/16/06